

**REMARKS**

**Status of the Claims:**

Claims 27 is amended, and claims 24, 27-28, and 33-49 are pending. Elected claims 24, 27-28, and 33 should be examined.

**Oath/Declaration:**

The Examiner is thanked for indicating that the application was filed with an unexecuted declaration. As Applicants are presently obtaining an executed declaration, Applicants respectfully request that this objection be held in abeyance.

**Rejections- 35 U.S.C. § 112, first paragraph:**

Claim 33 was rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. The PTO noted that “Applicants are in the process of depositing dMsh2-9 cell line. See Applicants amendment page 7, Section III.” Office Action, page 4. Furthermore, the PTO stated that “Applicants request that the rejection be held in abeyance until Applicants have provided the required affidavit or statement.” Office Action, page 4. However, the PTO noted that “Applicants request is noted, however a rejection can not be held in abeyance.” Office Action, page 4. Applicants respectfully traverse this rejection.

Biological material may be deposited at any acceptable depository during the pendency of a patent application. 37 C.F.R. § 1.804 (b). Where a deposit is needed for satisfying the requirements of 35 U.S.C. § 112, and the deposit is made during the pendency of the application, the deposit must be made no later than the time period set forth by the Examiner at the time the Notice of Allowance and Issue Fee Due is mailed. 37 C.F.R. § 1.809 (c). In other words, a necessary deposit need not be made by Applicant until the application is in condition for allowance so long as the applicant has provided a written statement asserting that an acceptable deposit will be made on or before payment of the issue fee. 37 C.F.R. § 1.809 (b). This written assurance must provide sufficiently detailed information to convince the Examiner that there is no outstanding issue regarding deposits that needs to be resolved. The written assurance should be accepted by the PTO if it clearly

states that an acceptable deposit will be made within the required time and under conditions which satisfy the PTO's rules. MPEP § 2411.02.

Accordingly, and as the PTO noted, "Applicants are in the process of depositing the dMsh2-9 cell line." Office Action, page 4. Therefore, the PTO has been provided a written assurance that an acceptable deposit will be made on or before payment of the issue fee. 37 C.F.R. § 1.809 (b). Thus, the rejection is improper and should be withdrawn.

**Rejections- 35 U.S.C. § 112, second paragraph**

Claims 27-28 are rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. Specifically, the Examiner stated that "claim 27 depends on canceled claim 26 and therefore it can not be determined what embodiments both claims 27 and claim 28 would encompass." Office Action, page 4. As the present version of the claims avoids this issue, the rejection should be withdrawn.

**Rejections- 35 U.S.C. § 103 (a)**

Claims 24, 27-28, and 32 were rejected under 35 U.S.C. § 103 (a) as allegedly unpatentable over Varlet et al., GenBank accession number X81143, and Berns et al. (U.S. Patent No. 5,789,215 or WO 93/04169) in view of Orth et al. (PNAS, 1994). Office Action, pages 7-10. Applicants respectfully traverse this rejection.

To properly combine references, there must be some teachings or suggestion in the prior art. MPEP § 2142. Thus, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. MPEP § 2143.01.

Furthermore, even if there were suggestion for such a combination, the combined teachings would not result in the claimed method. To establish a *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art.

MPEP § 2143.03.

Considering the disclosures as a whole, the cited references teach (i) mutations of Msh2 may lead to genetic instability of cancer and (ii) MSH2 only affects genes having microsatellite sequences. Therefore, considering the references in their entirety, the cited references teach away from the rejected claims. One of ordinary skill in the art would not have been motivated to combine the teachings of the references, and even if the teachings of the references were combined, the combined teachings would not render the present invention obvious.

According to the PTO, Varlet discloses “Msh2 in lower eukaryotes are associated with mismatch repair.” Office Action, page 7. While Varlet discloses that mutations or the absence of Msh2 may lead to a genetic instability or development of cancer, Varlet does not disclose that both Msh2 alleles must be mutated in order to obtain genetic instability. Admittedly, the PTO found that Varlet’s disclosure was “insufficient to conclude that disruption of both copies would be required for an observable phenotype.” Office Action, page 7. Accordingly, Varlet would not have rendered the present invention obvious, and the rejection should be withdrawn.

The PTO relied on Orth to remedy the deficiencies of Varlet. Specifically, the PTO stated that “Orth et al. teaches that in mammals, in particular humans, the characteristic of genetic instability in cell requires that both copies of MSH2 be disrupted.” Office Action, page 8. While Orth discloses that the source of the genetic stability in one ovarian tumor (out of 5 cell lines analyzed) is a point mutation in MSH2 gene, Orth teaches away from the present invention. Specifically, Orth teaches that a mutation in MSH2 only affects genes containing microsatellite sequences. See Orth, page 9498-9499. That is, Orth teaches disrupting both MSH2 alleles will not produce an overall mismatch repair deficiency phenotype unless the gene has a microsatellite sequence. As Orth teaches away from the present invention, Orth would not have remedied the deficiencies of Varlet.

Attempting to remedy the deficiencies of both Varlet and Orth, the PTO relied on Berns et al. (U.S. Patent No. 5,789,215 or WO 93/04169). The PTO stated that “both

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references by Berns et al. teach a method of generating transgenic animals wherein a gene of interest is disrupted." Office Action, page 9. While the Berns references provide one approach for modifying gene expression, Berns does not remedy the deficiencies of both Varlet and Orth. Accordingly, neither Berns reference, alone or in combination with both Varlet and Orth, would have rendered the present invention obvious. Because the combination of cited references does not render the claimed invention obvious, Applicants respectfully request withdrawal of the rejection.

### CONCLUSION

As the above-presented amendments and remarks address and avoid each rejection presented by the Examiner, withdrawal of each rejection and allowance of the claims are respectfully requested. No new matter has been added.

If there are any questions concerning this application, the Examiner is courteously invited to contact the undersigned counsel.

Respectfully submitted,

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